



4160-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2007-D-0369]

Draft Guidance for Industry on Bioequivalence Recommendations for Rifaximin Tablets;  
Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of two draft guidances for industry entitled "Bioequivalence Recommendations for Rifaximin," one for the 200-milligram (mg) strength (rifaximin-200) and one for the 550-mg strength (rifaximin-550). The recommendations provide specific guidance on the design of bioequivalence (BE) studies to support abbreviated new drug applications (ANDAs) for rifaximin tablets.

DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the Agency considers your comment on the draft guidances before it begins work on the final versions of the guidances, submit either electronic or written comments on the draft guidances by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

ADDRESSES: Submit written requests for single copies of the draft guidances to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the

SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance documents.

Submit electronic comments on the draft guidances to <http://www.regulations.gov>.

Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

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Center for Drug Evaluation and Research (HFD-600),  
Food and Drug Administration,  
7519 Standish Pl.,  
Rockville, MD 20855,  
240-276-8608.

SUPPLEMENTARY INFORMATION:

I. Background

In the Federal Register of June 11, 2010 (75 FR 33311), FDA announced the availability of a guidance for industry entitled “Bioequivalence Recommendations for Specific Products,” which explained the process that would be used to make product-specific BE recommendations available to the public on FDA’s Web site at

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm>.

As described in that guidance, FDA adopted this process as a means to develop and disseminate product-specific BE recommendations and provide a meaningful opportunity for the public to consider and comment on those recommendations. This notice announces the availability of two draft BE recommendations, one for rifaximin-200 and one for rifaximin-550.

Xifaxan (rifaximin) 200-mg tablets, approved by FDA in May 2004, are indicated for the treatment of patients ( $\geq 12$  years of age) with travelers' diarrhea caused by noninvasive strains of Escherichia coli. Xifaxan (rifaximin) 550-mg tablets, approved by FDA in March 2010, are indicated for reduction in risk of hepatic encephalopathy recurrence in patients  $\geq 18$  years of age. Xifaxan, 200 mg, and Xifaxan, 550 mg, are designated the reference listed drugs (RLDs) and therefore any ANDAs for generic rifaximin-200 or rifaximin-550 must demonstrate BE to the relevant RLD prior to approval. There are no approved ANDAs for these products.

In November 2011, FDA posted on its Web site a draft guidance for industry on the Agency's recommendations for BE studies to support ANDAs for rifaximin-200 (Draft Rifaximin-200 BE Recommendations). FDA is now issuing a draft guidance for industry on BE recommendations for generic rifaximin-550 (Draft Rifaximin-550 BE Recommendations).

In May 2008, Salix Pharmaceuticals, Inc. (Salix), manufacturer of the RLD, Xifaxan (200 mg), filed a citizen petition requesting that FDA refuse to receive for substantive review, or approve, ANDAs for generic rifaximin-200 unless the ANDAs contain certain data to demonstrate BE (Docket No. FDA-2008-P-0300). FDA is reviewing the issues raised in the petition and will consider any comments on the Draft Rifaximin-200 BE Recommendations before responding to Salix's citizen petition and finalizing its BE recommendations for rifaximin-200.

These draft guidances are being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidances, when finalized, will represent the Agency's current thinking on the design of BE studies to support ANDAs for rifaximin-200 and rifaximin-550. They do not create or confer any rights for or on any person and do not operate to bind

FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

## II. Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) either electronic or written comments regarding this document. It is only necessary to send one set of comments. It is no longer necessary to send two copies of mailed comments. Identify comments with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

## III. Electronic Access

Persons with access to the Internet may obtain the documents at either <http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/default.htm> or <http://www.regulations.gov>.

Dated: February 7, 2012.

Leslie Kux,

Acting Assistant Commissioner for Policy.